

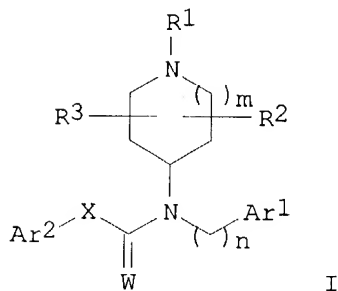
10/601,070

STM structure search  
93.04

=> d ibib abs hitstr 1-4

ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2004:451629 CAPLUS  
DOCUMENT NUMBER: 141:23543  
TITLE: Preparation of N-substituted piperidine derivatives as serotonin receptor agents  
INVENTOR(S): Andersson, Carl-Magnus; Schlienger, Nathalie; Fejzic, Alma; Hansen, Eva Louise; Pawlas, Jan  
PATENT ASSIGNEE(S): Swed.  
SOURCE: U.S. Pat. Appl. Publ., 44 pp.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

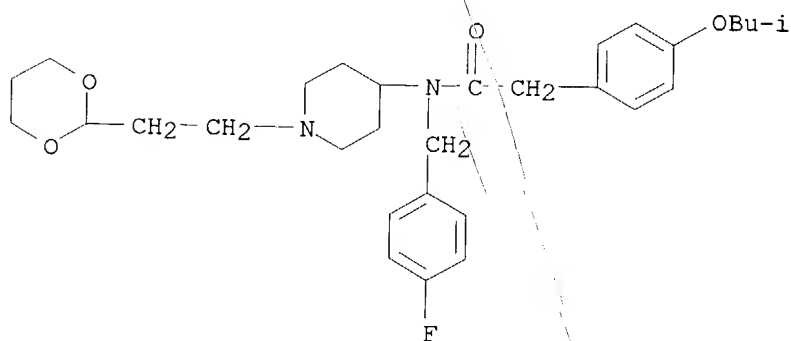
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004106600	A1	20040603	US 2003-601070	20030620
PRIORITY APPLN. INFO.:			DK 2002-973	A 20020624
			US 2002-391269P	P 20020624
OTHER SOURCE(S):	MARPAT 141:23543			
GI				



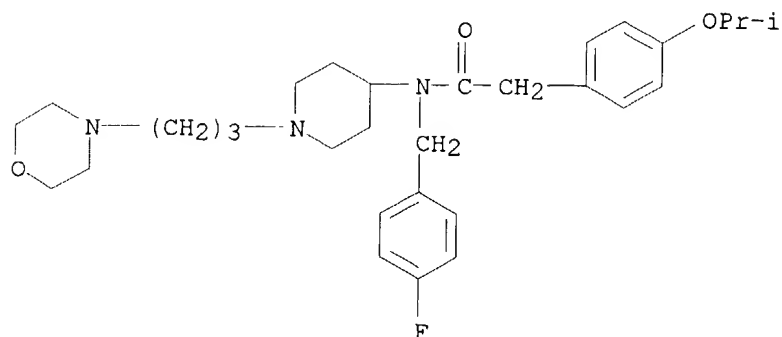
AB Disclosed herein are compds. of formula (I), pharmaceutically acceptable salts, amides, esters, or prodrugs thereof [wherein R1 = each (un)substituted heterocyclyl or heterocyclyl-C1-6 alkyl; R2, R3 = H, C1-6 alkyl, or halogen or such that R2 together with R3 forms a ring; m = 0, 1, 2; n = 1, 2, 3; Ar1 = each (un)substituted aryl or heteroaryl; W = O, S; X = each (un)substituted methylene, ethylene, propylene, or vinylene, CH2NR (wherein R = H, C1-6 alkyl); Ar2 = each (un)substituted aryl or heteroaryl]. Also disclosed are. (1) methods of inhibiting an activity of a monoamine receptor comprising contacting the monoamine receptor or a system containing the monoamine receptor with an effective amount of one or more of the compds. of formula I, (2) methods of inhibiting an activation of a monoamine receptor comprising contacting the monoamine receptor or a system containing the monoamine receptor with an effective amount of one or more of the compds. of formula I, and (3) methods of treating a disease condition associated with a monoamine receptor, in particular serotonin receptor 5-HT2A subclass. The disease condition is selected from (a) the group consisting of schizophrenia, schizoaffective disorders, psychosis, drug induced psychosis, and side effects observed with the treatment of chronic neurodegenerative disorders with a selective serotonin reuptake inhibitor (SSRI), wherein said neurodegenerative disorder is selected from

Alzheimer's disease, Parkinson's disease, Lewy body dementia, frontotemporal dementia, spinocerebellar atrophy, and Huntington's disease, and (b) the group consisting of Reynaud's Phenomena, migraine, hypertension, thrombosis, vasospasm, ischemia, depression, anxiety, motor tics, Tourette's syndrome, dyskinesias, on/off phenomena, tremor, rigidity, bradykinesia, psychomotor slowing, addiction, including alc. addiction, opioid addiction, and nicotine addiction, sleep disorders, appetite disorders, and decreases in libido and ejaculatory problems. Thus, N-(4-fluorobenzyl)-2-(4-isobutoxyphenyl)-N-[1-[3-(4-(S)-isopropyl-2-oxooxazolidin-3-yl)propyl]piperidin-4-yl]acetamide oxalate, which was prepared by alkylation of N-(4-fluorobenzyl)-2-(4-isobutoxyphenyl)-N-piperidin-4-ylacetamide with (4S)-3-(3-chloropropyl)-4-isopropylloxazolidin-2-one, inhibited 5-HT<sub>2A</sub> receptor by 104% in a receptor selection and amplification (R-SAT) assay using NIH3T3 cells.

- IT **639861-75-9P**, N-[1-[2-(1,3-Dioxan-2-yl)ethyl]piperidin-4-yl]-N-(4-fluorobenzyl)-2-(4-isobutoxyphenyl)acetamide **639862-90-1P**, N-[1-[2-(1,3-Dioxan-2-yl)ethyl]piperidin-4-yl]-N-(4-fluorobenzyl)-2-(4-isopropylphenyl)acetamide **639862-92-3P**, N-[1-[2-(1,3-Dioxan-2-yl)ethyl]piperidin-4-yl]-N-(4-fluorobenzyl)-2-(4-trifluoromethoxyphenyl)acetamide **639863-26-6P**, N-(4-Fluorobenzyl)-2-(4-isobutoxyphenyl)-N-[1-[3-(2-oxopiperidin-1-yl)propyl]piperidin-4-yl]acetamide  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (intermediate; preparation of N-substituted piperidine derivs. as serotonin receptor inhibitors for treating symptoms, diseases and disorders associated with monoamine receptors, including serotonin receptors)  
 RN 639861-75-9 CAPLUS  
 CN Benzeneacetamide, N-[1-[2-(1,3-dioxan-2-yl)ethyl]-4-piperidinyl]-N-[(4-fluorophenyl)methyl]-4-(2-methylpropoxy)- (9CI) (CA INDEX NAME)



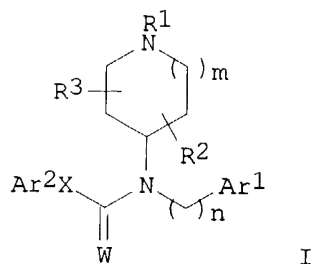
- RN 639862-90-1 CAPLUS  
 CN Benzeneacetamide, N-[1-[2-(1,3-dioxan-2-yl)ethyl]-4-piperidinyl]-N-[(4-fluorophenyl)methyl]-4-(1-methylethyl)- (9CI) (CA INDEX NAME)



*Answer*  
 L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 2004:2854 CAPLUS  
 DOCUMENT NUMBER: 140:77030  
 TITLE: Preparation of 1,4-disubstituted piperidines as serotonin 5-HT<sub>2A</sub> inverse agonists.  
 INVENTOR(S): Andersson, Carl-magnus; Schlienger, Nathalie; Fejzic, Alma; Hansen, Eva Louise; Pawlas, Jan  
 PATENT ASSIGNEE(S): Acadia Pharmaceuticals Inc., USA  
 SOURCE: PCT Int. Appl., 103 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000808	A2	20031231	WO 2003-US19797	20030620
WO 2004000808	A3	20040325		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

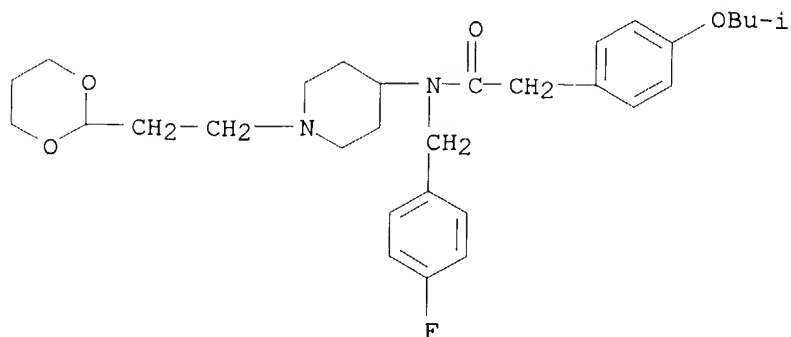
PRIORITY APPLN. INFO.: US 2002-391269P P 20020624  
 OTHER SOURCE(S): MARPAT 140:77030  
 GI



AB Title compds. [I; R1 = (substituted) heterocyclyl, heterocyclylalkyl; R2, R3 = H, alkyl, halo; R2R3 = atoms to form a ring; m = 0-2; n = 1-3; Ar1 = (substituted) aryl, heteroaryl; W = O, S; X = (substituted) methylene, ethylene, propylene, vinylene, CH<sub>2</sub>N(R<sub>n</sub>); R<sub>n</sub> = H, alkyl; Ar2 = (substituted) aryl, heteroaryl], were prepared. Thus, a mixture of N-(4-fluorobenzyl)-N-(piperidin-4-yl)-2-(4-isobutoxyphenyl)acetamide, K<sub>2</sub>CO<sub>3</sub>, NaI, and (4S)-3-(3-chloropropyl)-4-isopropylloxazolidinon-2-one were stirred overnight to give 71% N-(4-fluorobenzyl)-2-(4-isobutoxyphenyl)-N-[1-[3-(4-(S)-isopropyl-2-oxooxazolidin-3-yl)propyl]piperidin-4-yl]acetamide oxalate (117NLS01). The latter showed pIC<sub>50</sub> = 9.7 for repression of 5-HT<sub>2A</sub> receptor activity.

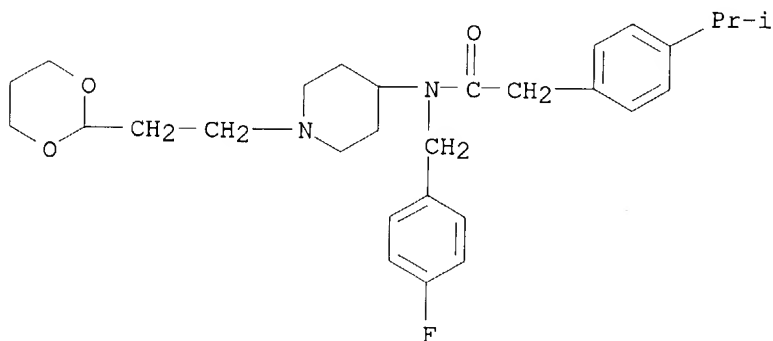
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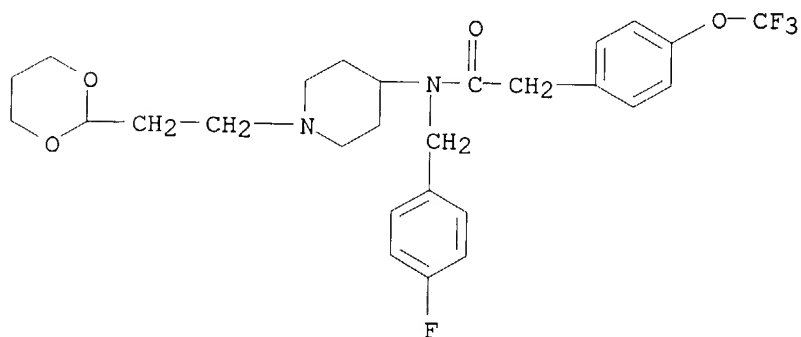
RN 639862-90-1 CAPLUS

CN Benzeneacetamide, N-[1-[2-(1,3-dioxan-2-yl)ethyl]-4-piperidinyl]-N-[(4-fluorophenyl)methyl]-4-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 639862-92-3 CAPLUS

CN Benzeneacetamide, N-[1-[2-(1,3-dioxan-2-yl)ethyl]-4-piperidinyl]-N-[(4-fluorophenyl)methyl]-4-(trifluoromethoxy)- (9CI) (CA INDEX NAME)



L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:836853 CAPLUS

DOCUMENT NUMBER: 139:337978

TITLE: Preparation of N-substituted pyridinone and pyrimidinone derivatives for use as Lp-PLA2 inhibitors in the treatment of atherosclerosis

INVENTOR(S): Leach, Colin Andrew; Smith, Stephen Allan

10/601,070

PATENT ASSIGNEE(S): Glaxo Group Limited, UK  
SOURCE: PCT Int. Appl., 38 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003086400	A1	20031023	WO 2003-GB1544	20030410
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: GB 2002-8279 A 20020410  
OTHER SOURCE(S): MARPAT 139:337978  
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The title compds. [I; R1 = (un)substituted aryl; R2 = halo, alkyl, alkoxy, etc.; R3 = H, halo, alkyl, hydroxyalkyl; R2 and R3 together with the pyridone or pyrimidone ring carbons to which they are attached form (un)substituted fused 5-6 membered carbocyclic ring, fused benzo or heteroaryl ring; R4 = alkyl substituted by 5-7 membered saturated heterocyclyl comprising N and optionally O or S; R5 = (un)substituted (hetero)aryl; R6 = (un)substituted (hetero)aryl; X = CH, N; Y = alkylene, CH:CH, (CH<sub>2</sub>)<sub>n</sub>S; n = 1-3] that are inhibitors of the enzyme Lp-PLA2 and are of use in therapy, in particular for treating atherosclerosis, were prepared. Thus, amidation of 2-[2-(2,3-difluorobenzylthio)-4-oxo-4H-quinolin-1-yl]acetic acid with N-(1-thiazol-2-ylmethylpiperidin-4-yl)-4'-trifluoromethylbiphen-4-ylmethylamine (prepns. given) afforded the quinolinone II. The exemplified compds. I showed IC<sub>50</sub> values in the range <0.1 to 100 nM against Lp-PLA2.

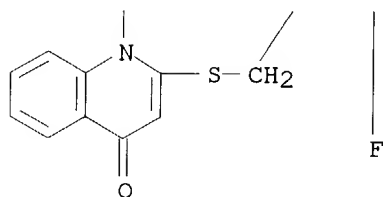
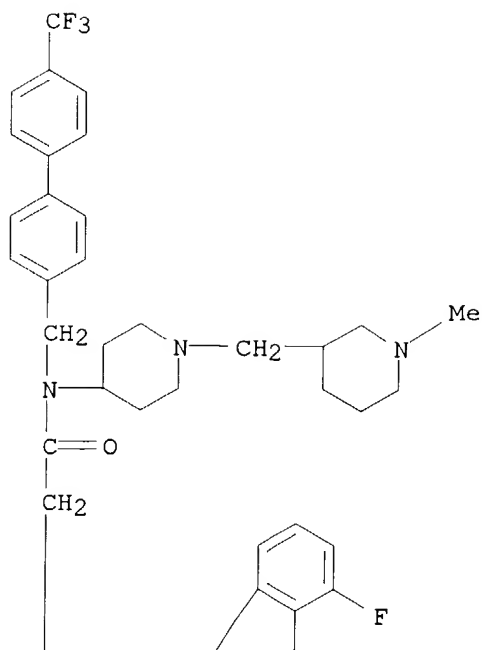
IT 615577-27-0P 615577-28-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

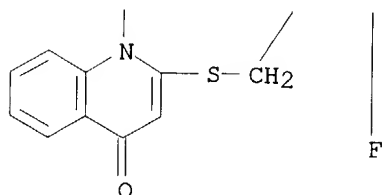
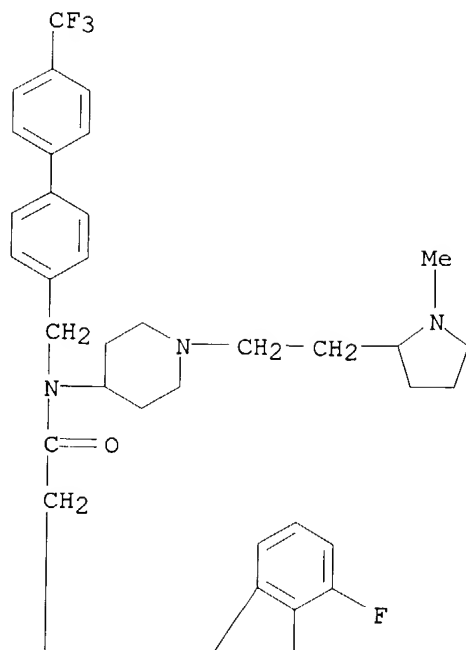
(preparation of pyridinone and pyrimidinone derivs. for use as Lp-PLA2 inhibitors in the treatment of atherosclerosis)

RN 615577-27-0 CAPLUS

CN 1(4H)-Quinolineacetamide, 2-[[[(2,3-difluorophenyl)methyl]thio]-N-[1-[(1-methyl-3-piperidinyl)methyl]-4-piperidinyl]-4-oxo-N-[[4'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]methyl]- (9CI) (CA INDEX NAME)



RN 615577-28-1 CAPLUS  
CN 1(4H)-Quinolineacetamide, 2-[[[2,3-difluorophenyl)methyl]thio]-N-[1-[2-(1-methyl-2-pyrrolidinyl)ethyl]-4-piperidinyl]-4-oxo-N-[[4'-(trifluoromethyl)[1,1'-biphenyl]-4-yl)methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

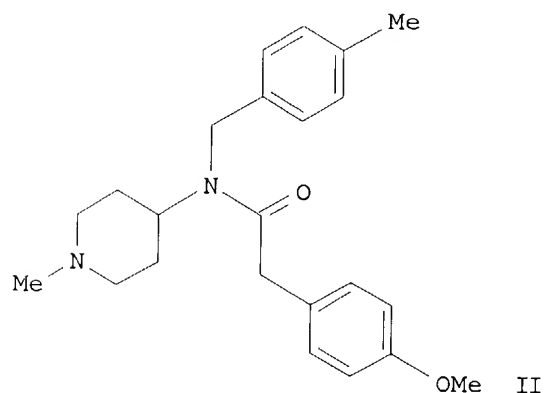
L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 2001:676749 CAPLUS  
 DOCUMENT NUMBER: 135:242140  
 TITLE: Preparation of N-piperidinyl-N-alkyl-acetamides and N,N,N'-substituted ureas as 5-HT2A inverse agonists/antagonists  
 INVENTOR(S): Andersson, Carl M.; Croston, Glenn; Hansen, E. L.; Uldam, A. K.  
 PATENT ASSIGNEE(S): Acadia Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 150 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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10/601,070

WO 2001066521 A1 20010913 WO 2001-US7187 20010306  
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CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID,  
IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,  
MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG,  
SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW,  
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
US 2002004513 A1 20020110 US 2001-800096 20010306  
EP 1263729 A1 20021211 EP 2001-914716 20010306  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
JP 2003531829 T2 20031028 JP 2001-565339 20010306  
BR 2001008977 A 20040106 BR 2001-8977 20010306  
ZA 2002005902 A 20031023 ZA 2002-5902 20020723  
US 2003220316 A1 20031127 US 2003-409782 20030407  
US 6756393 B2 20040629  
PRIORITY APPLN. INFO.: US 2000-187289P P 20000306  
US 2001-800096 A1 20010306  
WO 2001-US7187 W 20010306  
OTHER SOURCE(S): MARPAT 135:242140  
GI



AB Title compds. Ar1-Y2-Y1-N(Z)-C:W-X1-X2-Ar2 [Z = NR-substituted piperidinyl, tropanyl, azetidiny, etc.; R = H, cyclic/straight-chain acyclic organyl group, hydroxyalkyl, aminoalkyl, aralkyl or heteroaralkyl group; X1 = CH2, vinylene, NH or N-alkyl; X2 = CH2, or, when X1 = CH2 or vinylene, X2 = CH2 or a bond; or when X1 is CH2, X2 = O, S, NH, N(lower alkyl) or a bond; Y1 = CH2 and Y2 = CH2, vinylene, ethylene, propylene, bond; or Y1 = bond and Y2 = vinylene; or Y1 = ethylene and Y2 = O, S, NH, N(lower alkyl); Ar1 and Ar2 = (un)substituted (hetero)aryl provided that Ar1 and Ar2 are not simultaneously phenyl; W = O, S; I] were prepared. Examples include over 130 compds. synthesized, 5 serotonin receptor binding assays and 3 in-vivo models. For instance, 4-methylbenzylamine was reductively alkylated with 1-methyl-4-piperidone (MeOH, HOAc, NaCNBH3, 20 h., room temperature). The resulting amine was alkylated with 4-methoxyphenylacetyl chloride (DCM, 4 h., room temperature) to give II, isolated as the hydrochloride salt and subsequently purified by chromatog. Many of the examples had pIC50 (-log IC50) = 7.8 - 9.0 for HT2A. I are

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used for the treatment of disease in which modification of serotonergic receptor activity has a beneficial effect.

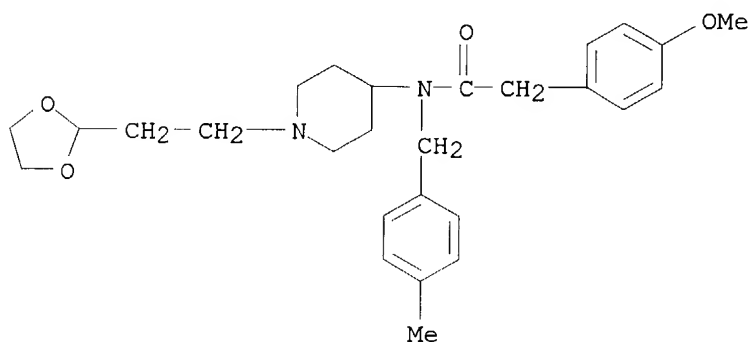
IT **359881-45-1P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug; preparation of N-piperidinyl-N-alkyl-aryl-acetamides and N,N,N'-substituted ureas as 5-HT<sub>2A</sub> inverse agonists)

RN 359881-45-1 CAPLUS

CN Benzeneacetamide, N-[1-[2-(1,3-dioxolan-2-yl)ethyl]-4-piperidinyl]-4-methoxy-N-[(4-methylphenyl)methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

2

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L3 205 S L1 FULL

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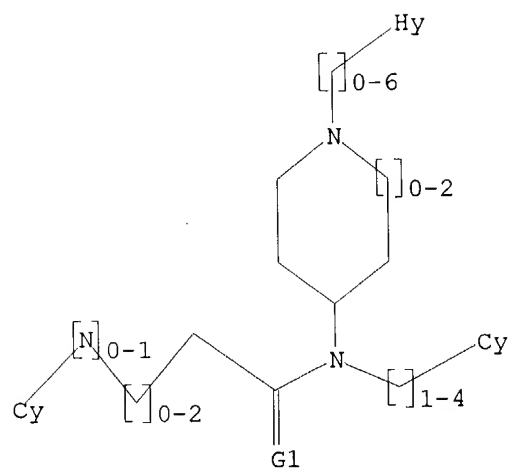
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L1 HAS NO ANSWERS

L1 STR

10/601,070



G1 O,S

Structure attributes must be viewed using STN Express query preparation.

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